2H), 5.99 (s, 1H), 5.94 (s, 1H), 5.10 (d, J=17.3 Hz, 1H), 4.98 (d, J=17.1 Hz, 1H), 4.93 (s, 2H), 4.78 (s, 1H) 3.99 (dd, J=22.3, 3.7 Hz, 1H), 3.78-3.63 (m, 1H), 3.70 (s, 6H)

EXAMPLE 8

Synthesis of (5S)-5-[3,5-dihydroxy-4-(4-methyl-benzyloxy)-phenyl]-5,9-dihydro-8H-furo[3',4':6,7] naphtho[2,3-d][1,3]dioxol-6-one (Compound 1-14)

[0051] To a stirred solution of 4'-demethyl-β-apopicropodophyllin (200 mg, 0.52 mmol) in anhydrous N,N-dimethylformamide (2 mL) was added sodium hydride (25 mg, 60%, 0.62 mmol) at below 0° C. After the mixture was stirred at same temperature for 1 hr, 4-methylbenzyl bromide (140 mg, 0.78 mmol) was added dropwise to the mixture. The reaction mixture was stirred at room temperature for 2 hrs, quenched with water (20 mL) and extracted with ethyl acetate (2×10 mL). The combined organic layer was washed twice with water (10 mL), dried over $MgSO_4$ and concentrated in vacuo. The concentrate was purified by column chromatography on silica gel (ethyl acetate/n-hexane:1/2) to afford 157 mg (55%) of the desired product.

[0052] NMR (DMSO) δ (ppm): 7.31 (d, J=7.9 Hz, 2H), 7.15 (d, J=7.9 Hz, 2H), 6.88 (s, 1H), 6.81 (s, 1H), 6.48 (s, 2H), 5.99 (s, 1H), 5.94 (s, 1H), 5.10 (d, J=17.3 Hz, 1H), 4.98 (d, J=17.5 Hz, 1H), 4.76 (s, 2H), 3.99 (dd, J=22.1, 4.2 Hz, 1H), 3.76-3.73 (m, 1H), 3.71 (s, 6H), 2.29 (s, 3H)

[0053] [Anti-Cancer Effect in Cancer Cell Line]

[0054] 1) Cell Culture

[0055] Human lung cancer cells A549, NCl-H460 and 7 cancer cell lines were cultured in RPMI 1640 medium containing 10% FBS (Gibco, USA) and 1% penicillin-streptomycin. Human colon cancer cell HCT-116 cell line was cultured in McCoy's 5A medium containing 10% FBS (Gibco, USA) and 1% penicillin-streptomycin. Human leukemia cancer cell HL-60 cell line was cultured in IMDM medium containing 20% FBS (Gibco, USA) and 1% penicillin-streptomycin. Human normal cell line WI-38 was cultured in MEM containing 10% FBS (Gibco, USA), 1% penicillin-streptomycin, and 1% Non-Essential Amin Acids solution. Human normal cell line HUVEC cultured in Human Endothelial Growth Medium containing. All the cells were cultured in sterilized cell culture plastic dishes or 96-well plastic plates in a humidified incubator filled with 95% air and 5% CO_2 gas and maintained at a temperature of 37° C.

[0056] 2) Test Method

[0057] First, the cells are seeded in a 96-well plate (Nunc, 165305) at a volume of 100 μl, and then cultured in an incubator overnight to confirm that they grow well on the plate. Depending on the concentration of the drugs, each well is treated with 100 μl of the compound and then incubated to allow cells and compounds to react for 48 hrs. PrestoBlue Cell Viability Reagent (Invitrogen, A13262) was added to the compound-treated well, and then the plates were incubated in a humidified incubator at 37° C. for 30 mins. Each well was measured at a fluorescence detected with the wavelength of an excitation of 560 nm and an emission of 590 nm using by microplate reader (BioTek, Synergy H1). The IC_{50} value is calculated by using the Gen5 software.

[0058] The IC_{50} value of the compound in the present invention and positive control Etoposide describe in Table 3 and 4.

TABLE 3

IC50 values for 48 h (unit; μM)

	cell line	Etoposide	example 1	example 2	example 3	example 4
lung	A549	2.159	0.065	0.202	0.127	0.698
	H460	0.971	0.06	0.134	0.174	0.796
	H1299	40.12	>50	>50	>50	—
	H1650	>50	>50	>50	>50	—
	H1975	>50	>50	>50	>50	—
	HCC827	>50	>50	>50	>50	—
	H146	>50	>50	>50	>50	—
breast	MCF-7	>50	>50	>50	>50	—
	MDA-MB-231	>50	>50	>50	>50	>50
colon	HCF116	7.289	0.129	1.392	0.234	1.57
leukemia	HL-60	2.43	0.03	0.25	0.181	>50
	K562	—	>50	>50	>50	0.398
pancreas	CFPAC-1	42.02	>50	>50	>50	—
	BxPC-3	>50	>50	>50	>50	—
normal	WI-38	>50	>50	>50	>50	>50
	WI-26	—	>50	>50	>50	—
	HUVEC	>50	>50	>50	>50	>50

TABLE 4

IC50 values for 48 h(unit; μM)

	cell line	Etoposide	example 5	example 6	example 7	example 8
lung	A549	2.159	>50	0.288	>50	>50
	H460	0.971	>50	0.437	>50	>50
	H1299	40.12	—	—	—	—
	H1650	>50	—	—	—	—